REMARKS

In the Office Action dated December 19, 2002, Claims 1-9 and 11-21 are currently under examination.

In the Office Action Claims 3-8, 11, 12, and 17-21 have been rejected under 35 U.S.C. §112, second paragraph, as allegedly failing to particularly point out and distinctly claim the subject matter of the invention. Claims 13-21 have been rejected under 35 U.S.C. §103(a) as allegedly unpatentable over O'Malley et al., U.S. Patent No. 5,494,908 (hereinafter "O'Malley '908"). Additionally, Claims 1 –21 have been rejected under the judicially created doctrine of obviousness-type double patenting, as allegedly unpatentable over Claims 1 and 2 of Villalobos et al., U.S. Patent No. 5,538,984 (hereinafter "Villalobos '984").

This response addresses each of the Examiner's rejections. Accordingly, the present application is in condition for allowance. Favorable consideration of all pending claims is respectfully requested.

Initially, applicants draw the Examiner's attention to the amendments to Claims 11, 13, 17, and 19 –21. Claim 11 has been amended to depend from Claim 1. Claim 13 has been amended to conform the definitions of substituents in Formula I of Claim 13 with those of Formula I in Claim 1. Claims 17 and 19 –21 have been amended to remove the limitation "Formula I."

No new matter has been added.

In the Office Action Claims 3-8, 11, 12, and 17-21 have been rejected under 35 U.S.C. §112, second paragraph, as allegedly failing to particularly point out and distinctly claim the subject matter of the invention. In Paragraph 10 of the Office

Action Claims 3-8, 11, 12, and 17-21 were rejected under 35 U.S.C. §112, second paragraph. In Paragraphs 11 and 12 the Examiner explained the bases for the rejections of Claims 17-21 and 11, respectively. Because no substantive defect in Claims 3-8 or 12 was specifically alleged, applicant assumes that the inclusion of Claims 3-8 and 12 in Paragraph 10 was an error.

The Office Action has rejected Claims 17-21 under 35 U.S.C. §112, second paragraph, alleging insufficient antecedent basis for the limitation "Formula I" in this claim. In accordance with the Examiner's suggestion, these claims have been made to depend on Claim 1, which incorporates the embodiments of Formula I. Therefore, the rejection of Claims 17-21 under 35 U.S.C. §112, second paragraph, has been overcome, and withdrawal thereof is respectfully requested.

The Office Action has rejected Claim 11 under 35 U.S.C. §112, second paragraph, pointing out that Claim 11 was dependent on cancelled Claim 10. Accordingly, Claim 11 has been amended to depend on Claim 1. Therefore, the rejection of Claim 11 under 35 U.S.C. §112, second paragraph, is overcome, and withdrawal thereof is respectfully requested.

The Office Action has rejected Claims 13-21 under 35 U.S.C. §103(a) as allegedly unpatentable over O'Malley '908. The Examiner has alleged that the compound of Formula I is obvious in view of the compound disclosed by O'Malley in column 4, line 50, to column 5, line 34. In conforming the definitions of substituents in Formula I of Claim 13 with those of Formula I in Claim 1, applicants have amended Claim 13 to exclude the possibility of an amino group at the 3-position. Therefore, the

rejection of Claims 13-21 under 35 U.S.C. §103(a) has been overcome, and withdrawal thereof is respectfully requested.

Additionally, Claims 1 –21 have been rejected under the judicially created doctrine of obviousness-type double patenting, as allegedly unpatentable over Claims 1 and 2 of Villalobos et al., U.S. Patent No. 5,538,984 (hereinafter "the '984 patent"). Applicant respectfully submits that the Examiner has not met the burden of establishing a *prima facie* case of obviousness-type double patenting.

The Examiner has alleged that Claims 1 and 2 of the '984 patent are directed to enhancing memory or treating Alzheimer's disease. In partial support of the assertion that Claims 1 – 21 of the present invention are not patentably distinct from Claims 1 and 2 of the '984 patent, the Examiner has merely asserted that "it is well established in the art that both dementia as well as Alzheimer's Disease are commonly associated with disorders afflicting older mammals." Applicant respectfully submits that the Examiner is making the unstated and unfounded assumption that cognitive disorders in non-human mammals are necessarily connected with Alzheimer's Disease.

Applicant respectfully observes that the Examiner's assertion could be made with respect to almost any affliction, since older mammals are known to be more vulnerable to a host of disorders, from influenza to cancer. Applicant further respectfully submits that the nexus between one type of disease and the population that the Examiner identified does not automatically bear on the treatment of other diseases in mammals, no less companion animals.

As indicated in the attached materials (Exhibit A), there is a wide variety of other afflictions which may impact on cognition or on behavior, even though the

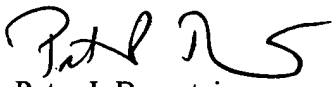
public is perhaps most familiar with Alzheimer's disease. As shown, dementia in humans has been attributed to such distinct diseases as Parkinson's disease, Diffuse Lewy Body disease, multi-infarct dementia, subcortical vascular dementia, Pick's disease, and Huntington's disease. None of these afflictions are mentioned in the '984 patent. Moreover, the '984 patent lacks any suggestion or motivation to employ its treatment strategy for behavioral disorders in companion animals.

Since the study of dementia in humans is still in its infancy, it follows that the study in companion animals of aged-related cognitive dysfunction syndrome, as defined on page 1 of the specification, is even less advanced. The present invention teaches the use of the claimed compounds to treat, in companion animals, age-related behavioral disorders from a wide variety of etiologies apart from Alzheimer's disease. Applicant respectfully submits that without additional support beyond the assertion that dementia and Alzheimer's disease are commonly associated with afflictions in older mammals (i.e., humans) and the unsubstantiated suggestion that age-related disorders in companion animals are necessarily connected with Alzheimer's disease in humans, the Examiner has not met the burden of establishing a *prima facie* case of obviousness-type double patenting. Applicant respectfully requests reconsideration and withdrawal of the rejection made on this basis.

Attached hereto is a marked-up version of the changes made to the claims by the current amendment. The attached page is captioned "VERSION WITH MARKINGS TO SHOW CHANGES MADE."

Thus, in view of the foregoing amendments and remarks, the present application is in condition for allowance, which action is earnestly solicited.

Respectfully submitted,



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Enclosure

"VERSION WITH MARKINGS SHOWING CHANGES MADE"

IN THE CLAIMS

Claims 11, 13, 17 and 19-21 have been amended as follows:

11. (Twice amended) The method of Claim ~~10~~ 1 wherein the compound of Formula 1 is selected from the group consisting of:

5,7-dihydro-7-methyl-3-[2-[1-(phenylmethyl)-4-piperidinyl]ethyl]-6H-pyrrolo[4,5-f]-1,2-benzisoxazol-6-one;

5,7-dihydro-7-ethyl-3-[2-[1-(phenylmethyl)-4-piperidinyl]ethyl]-6H-pyrrolo[4,5-f]-1,2-benzisoxazol-6-one;

5,7-dihydro-3-[2-[1-(2-chloro-5-thiophenemethyl)-4-piperidinyl]ethyl]-6H-pyrrolo[4,5-f]-1,2-benzisoxazol-6-one;

5,7-dihydro-3-[2-[1-(2-methyl-4-thiazolemethyl)-4-piperidinyl]ethyl]-6H-pyrrolo[4,5-f]-1,2-benzisoxazol-6-one;

3-[2-[1-(3-bromophenylmethyl)-4-piperidinyl]ethyl]-5,7-dihydro-6H-pyrrolo[4,5-f]-1,2-benzisoxazol-6-one;

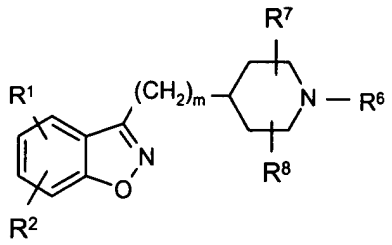
3-[2-[1-(4-bromophenylmethyl)-4-piperidinyl]ethyl]-5,7-dihydro-6H-pyrrolo[4,5-f]-1,2-benzisoxazol-6-one;

5,7-dihydro-3-[3-[1-(phenylmethyl)-4-piperidinyl]propyl]-6H-pyrrolo[4,5-f]-1,2-benzisoxazol-6-one;

6,8-dihydro-3-[2-[1-(phenylmethyl)-4-piperidinyl]ethyl]-7H-pyrrolo[5,4-g]-1,2- benzisoxazol-7-one; and

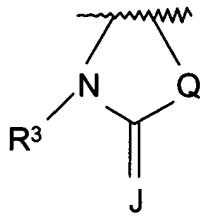
5,7-dihydro-3-[2-(1-(phenylmethyl)-4-piperidinyl]ethyl]-6H-pyrrolo[4,5-f]-1,2-benzisoxazol-6-one.

13. (Twice amended) A pharmaceutical composition for use in the treatment of an age-related behavior disorder in a companion animal comprising a compound of Formula 1:



Formula 1

wherein R^1 and R^2 are each independently selected from the group consisting of hydrogen; (C_1-C_6)alkoxy; benzyloxy; phenoxy; hydroxy; phenyl; benzyl; halo; nitro; cyano; -COR^5; -$COOR^5$; $CONHR^5$; -NR^5R^6; -NR^5COR^6; -$OCONR^5R^6$; -$NHCOOR^5$; (C_1-C_6) alkyl which may be substituted with from 1 to 3 fluorine atoms; SO_pCH_2-phenyl or SO_p(C_1-C_6) alkyl, wherein p is 0, 1 or 2; pyridylmethyloxy or thienylmethyloxy; 2-oxazolyl; 2-thiazolyl; and benzenesulfonamide; wherein the phenyl moieties of said phenoxy, benzyloxy, phenyl, benzyl and benzenesulfonamide groups, the pyridyl and thienyl moieties of said pyridylmethyloxy or thienylmethyloxy groups, and the oxazolyl and thiazolyl moieties of said 2-oxazolyl and 2-thiazolyl groups may be substituted with 1 or 2 substituents independently selected from the group consisting of halo, (C_1-C_4) alkyl, trifluoromethyl, (C_1-C_4) alkoxy, cyano, nitro and hydroxy; or R^1 and R^2 are attached to adjacent carbon atoms and form, together with the carbon atoms to which they are attached, a group of Formula 2:



Formula 2

wherein R^3 is hydrogen or (C_1-C_6) alkyl; J is oxygen, sulfur or NR^4; R^4 is hydrogen or (C_1-C_4) alkyl; and *Q* is oxygen, sulfur, NH, $CHCH_3$, $C(CH_3)_2$, -CH=CH-, or $(CH_2)_1$ wherein 1 is an integer from 1 to 3;

X is oxygen or sulfur;

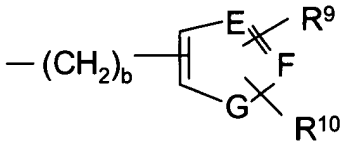
Y is (CH_2)m, CH=CH(CH_2)-, ~~$NR^4(CH_2)_m$~~, or -$O(CH_2)_m$-, wherein n is an integer from 0 to 3, and m is an integer from 1 to 3;

R^5 and R^6 are each independently selected from the group consisting of hydrogen, (C_1-C_6) alkyl, phenyl, and benzyl, wherein the phenyl moieties of said phenyl and benzyl groups may be substituted with 1 or 2 substituents independently selected from the group consisting of fluoro, chloro, bromo, iodo, (C_1-C_4) alkyl, trifluoromethyl, (C_1-C_4) alkoxy, cyano, nitro and hydroxy; or

NR^5R^6 together form a 4 or *5* membered ring wherein one atom of the ring is nitrogen and the others are carbon, oxygen or nitrogen; or NR^5COR^6 together form a 4 or 5

membered lactam ring;

L is phenyl, phenyl-(C_1-C_6) alkyl, cinnamyl or pyridylmethyl, wherein the phenyl moieties of said phenyl and phenyl-(C_1-C_6) alkyl may be substituted with 1 to 3 substituents independently selected from the group consisting of (C_1-C_6) alkyl, (C_1-C_6) alkoxy, (C_1-C_4) alkoxycarbonyl, (C_1-C_6)alkylcarbonyl, -$OCONR^5R^6$, -$NHCOOR^5$, and halo; or L is a group of Formula 3:



Formula 3

wherein b is an integer from 1 to 4; R^9 and R^{10} are independently selected from the group consisting of hydrogen, (C_1-C_4) alkyl, halo, and phenyl; E and F are independently -CH- or nitrogen; and G is oxygen, sulfur or NR^4, with the proviso that when E and F are both nitrogen, one of R^9 and R^{10} is absent; and

R^7 and R^8 are independently selected from the group consisting of hydrogen, (C_1-C_6) alkyl, (C_1-C_6) alkoxycarbonyl, (C_1-C_6) alkylcarbonyl, and (C_1-C_6) alkoxy, with the proviso that said (C_1-C_6) alkoxy is not attached to a carbon that is adjacent to a nitrogen; or a pharmaceutically acceptable salt of solvate thereof, and a pharmaceutically

acceptable carrier.

17. (Amended) A dosage form of a compound of ~~Formula~~ Claim 1 for use in the treatment of an age-related behavioral disorder in a companion animal.

19. (Twice amended) The dosage form of Claim 18 wherein the compound of ~~Formula I~~ Claim 1 is selected from the group consisting of:

5,7-dihydro-7-methyl-3-[2-[1-(phenylmethyl)-4-piperidinyl]ethyl]-6H-pyrrolo[4,5-f]-1,2-benzisoxazol-6-one;

5,7-dihydro-7-ethyl-3-[2-[1-(phenylmethyl)-4-piperidinyl]ethyl]-6H-pyrrolo[4,5-f]-1,2-benzisoxazol-6-one;

5,7-dihydro-3-[2-[1-(2-chloro-5-thiophenemethyl)-4-piperidinyl]ethyl]-6H-pyrrolo[4,5-f]-1,2-benzisoxazol-6-one;

5,7-dihydro-3-[2-[1-(2-methyl-4-thiazolemethyl)-4-piperidinyl]ethyl]-6H-pyrrolo[4,5-f]-1,2-benzisoxazol-6-one;

3-[2-[1-(3-bromophenylmethyl)-4-piperidinyl]ethyl]-5,7-dihydro-6H-pyrrolo[4,5-f]-1,2-benzisoxazol-6-one;

3-[2-[1-(4-bromophenylmethyl)-4-piperidinyl]ethyl]-5,7-dihydro-6H-pyrrolo[4,5-f]-1,2-benzisoxazol-6-one;

5,7-dihydro-3-[3-[1-(phenylmethyl)-4-piperidinyl]propyl]-6H-pyrrolo[4,5-f]-1,2-benzisoxazol-6-one;

6,8-dihydro-3-[2-[1-(phenylmethyl)-4-piperidinyl]ethyl]-7H-pyrrolo[5,4-g]-1,2- benzisoxazol-7-one; and

5,7-dihydro-3-[2-(1-(phenylmethyl)-4-piperidinyl]ethyl]-6H-pyrrolo[4,5-

f]-1,2-benzisoxazol-6-one.

20. (Twice amended) The dosage form of Claim 19 wherein the compound of ~~Formula I~~ Claim 1 is 5,7-dihydro-3-[2-(1-(phenylmethyl)-4-piperidinyl]ethyl]-6H-pyrrolo[4,5-f]-1,2-benzisoxazol-6-one.

21. (Amended) The dosage form of claim 20 wherein said dosage form comprises from about 0.001 mg to about 100 mg of the compound of ~~Formula I~~ Claim 1.